REMARKS

In view of the above amendment and the following remarks, the Examiner is requested to allow Claims 2-5, 27, and 37-40, the only claims pending and under examination in this application.

Formal Matters

Claims 1, 21, 27, 31, and 36 have been amended in response to the 35 U.S.C. § 112 rejection, and these amendments are discussed in greater detail below. Support for these amendments may be found throughout the specification and claims as originally filed, for example, on page 6, paragraph 0027, and on pages 7-8, paragraph 0030. Support for New Claims 37-40 may be found, for example, at paragraphs 0058, 0061, 0064, 0068, and 0072. As no new matter has been added by way of these amendments, entry thereof by the Examiner is respectfully requested.

Withdrawn Rejections – 35 U.S.C. §§ 102, 112

The Applicants acknowledge and thank the Examiner for the withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, as well as for the withdrawal of those under 35 U.S.C. § 102(a) over Mizushina et al. *Biochem. Biophys. Res. Commun.* **2003,** 301(2), 480-487.

Claim Rejections – 35 U.S.C. § 112

Claims 2-5 and 27 have been rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

Specifically, the Examiner states that it is unclear what is meant by the phrase "at least uncertain" and that it is therefore unclear what the scope of this claim limitation is in the context of the invention. The Examiner states that "at least" implies a scale, and the bounds of the scale are unclear.

Claim 27 has been amended by striking the words, "at least." Therefore, a scale is no longer implied, and the Applicants submit that this amendment renders the rejection moot. Accordingly, the Applicants respectfully request the withdrawal of this rejection.

Claim Rejections – 35 U.S.C. § 102

Claims 2-5 and 27 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Bailey et al. *Genet. Eng. News.* **2003,** 23(19), 32, 36-37. The Examiner asserts that the cited reference teaches each and every element of the claims.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The instant claims are directed to, *inter alia*, a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase under chromatographic conditions, in which the specificity of the first stationary phase for at least one constituent present in the sample is uncertain, and the specificity of the second stationary phase for the at least one constituent is certain, to at least determine the binding identity of the at least one constituent. It is not seen where this is taught by Bailey.

Bailey describes the use of a column with antibodies fixed to a solid phase to remove known high-concentration proteins from serum. Bailey states that the Multiple Affinity Removal System was designed to "specifically and simultaneously remove six high-abundance proteins in human serum" (Bailey, page 32, second column).

The Applicants respectfully submit that all of the antibodies in the column described by Bailey are of known specificity to serum proteins, which serum proteins are listed in Figure 1 on page 32 of Bailey. All of the antibodies of Bailey are known and demonstrated to bind their targets with high specificity (Bailey, page 32, paragraph spanning columns 3-4, and throughout the reference). Accordingly, Bailey is silent regarding a first stationary phase in which the specificity of the first stationary phase for at least one constituent present in the sample is uncertain, as is claimed.

The Examiner contends that the sentence bridging pages 36 and 37 of Bailey, "Table 1 (p. 32) shows the proteins identified from the retained fraction by the affinity column," proves that "the antibodies had unknown specificity to the serum proteins prior to the experiments disclosed in the article" (page 6 of Office Action). The Applicants respectfully disagree.

First, the Applicants note that a table showing proteins identified from a retained fraction in no way implies that the antibodies had unknown specificity to the serum proteins prior to the experiments disclosed in the article. In particular, the Applicants direct the Examiner's attention to column 3 of page 32, where Bailey discloses that the specificity of the antibodies for the serum proteins was known:

> [The system] was developed **to specifically and simultaneously remove six high-abundance proteins** . . . . The system was designed **for thorough, efficient removal** of multiple targeted proteins . . . . The **immunochemistry used makes the system highly specific** to the six human high-abundance proteins . . . .

(emphasis added). The Applicants submit that if antibodies were selected during the design of the column to specifically and efficiently remove the six high-abundance proteins, then the specificity of those antibodies for certain proteins must have been known.

Moreover, the Applicants contend that the Examiner is conflating the relevancy of the certainty of specificity. In the method of using Bailey's column, the specificity of the six human high-abundance proteins for the antibodies in the column

is certain. While there was some time in the past prior to November 2003 when the specificities of the antibodies for these proteins were uncertain, in the method of using Bailey's column, the specificity is certain.

By contrast, one element of the method of the instant claims is that it is a method of evaluating the specificity of said first stationary phase for at least one constituent present in the sample. Thus, in the method of using the instant invention, the specificity of the first stationary phase for the at least one constituent present in the sample is uncertain. Accordingly, Bailey does not teach each and every element of the claim limitations.

For this reason alone, the rejection may be withdrawn.

The Examiner asserts that paragraphs 3-5 on page 37 of Bailey disclose sequentially contacting a sample with a first stationary phase and then a second stationary phase.

However, the sequential contact disclosed by Bailey does not meet the limitation of the instant claims of a method of evaluating the specificity of a first stationary phase for at least one constituent present in the sample. Paragraphs 3-5 on page 37 of Bailey describe how the sequential two-column method is designed "[t]o assess how many proteins bind **nonspecifically** to material based on immobilized Cibacron Blue . . . ." (emphasis added). Hence, the sequential contact is for the purpose of determining which serum proteins that are not supposed to be bound by the Cibacron Blue column are in fact bound, for the purpose of demonstrating the greater specificity (and therefore superiority) of Bailey's column over the Cibacron Blue column. But this is not for the purpose of evaluating the specificity of a first stationary phase for at least one constituent present in the sample.

Accordingly, Bailey fails to teach at least these elements of the claims, and the rejection may be withdrawn.

Claims 2-5 and 27 have been rejected under 35 U.S.C. 102(b) as being anticipated by Jindal et al. U.S. Pub. No. 2002/0150926. The Examiner asserts that the cited reference teaches each and every element of the claims.

The instant claims are directed to, *inter alia*, a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase under chromatographic conditions, in which the specificity of the first stationary phase for at least one constituent present in the sample is uncertain, and the specificity of the second stationary phase for the at least one constituent is certain, to at least determine the binding identity of the at least one constituent. It is not seen where this is taught by Jindal.

The Applicants submit that the Examiner with respect to this rejection, too, has conflated the relevancy of the certainty of specificity. Jindal teaches a method of multi-dimensional systems, for screening libraries to select, recover and characterize a candidate ligand with a desired or preselected affinity K for a preselected target molecule (Jindal, paragraph 11). Jindal repeatedly emphasizes, throughout the specification, that the method taught therein is one for selecting or screening ligands based on their affinity for a target. Consider, for example: "[T]he practitioner is able to select a ligand . . . . This ability is especially relevant in drug screening applications . . ." (Jindal, paragraph 115); "[T]he practioner can use the methods of the invention to screen ligands for their ability to bind to a certain first target molecule, and their inability to bind to a second target" (Jindal, paragraph 119); "Thus, one may select for a ligand which will interfere with the binding activity of the natural ligand/target pair" (Jindal, paragraph 123) (all emphases added).

Thus, while after conducting Jindal's method one might have ligands having a specificity for some target molecule that is certain, before and during the execution of Jindal's method the specificity of any stationary phase for any ligand (i.e. constituent) is uncertain; screening methods inherently require uncertainty of specificity. If there were certainty of specificity, there would be no need to screen.

By contrast, in the instant invention, the specificity of the secondary stationary phase for the at least one constituent is certain before and during the execution of the method.

The Examiner asserts that paragraph 122 of Jindal teaches a first stationary phase with a specificity for at least one constituent present in the sample that is uncertain and a second stationary phase with a specificity for said at least one constituent in the sample that is certain. The Applicants respectfully submit that paragraph 122 teaches a sequential system wherein the first column is a size exclusion chromatography (SEC) system. SEC columns by definition slow the progression through the column of the smaller constituents within a sample. Because SEC columns discriminate between constituents based on size, and because all constituents have some size, the stationary phase of the SEC column affects all constituents. Therefore, the SEC column cannot have specificity for any constituent of a sample. Accordingly, Jindal's paragraph 122 does not teach a method where both stationary phases have some specificity—whether certain or uncertain—for a constituent.

As such, Jindal fails to teach a method in which the specificity of the first stationary phase for at least one constituent present in the sample is uncertain, and the specificity of the second stationary phase for the at least one constituent is certain.

Since Jindal fails to teach the claimed stationary phase with a specificity for at least one constituent present in the sample which is certain, Jindal further fails to teach a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase, where the specificities are respectively uncertain and certain. Jindal nowhere teaches any combination of targets in a column one of which is known to bind a ligand and one of which is not known to bind, much less such targets in any particular sequence.

Accordingly, Jindal fails to teach at least these elements of the claims, and the rejection may be withdrawn.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10030532-1.

Respectfully submitted,

Date: August 12, 2008

By: /Bret E. Field, Reg. No. 37,620/
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